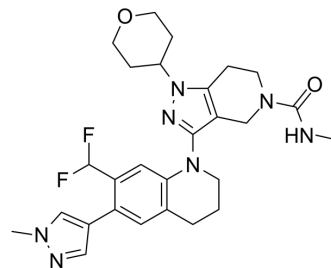


GNE-781

Cat. No.:	HY-108696
CAS No.:	1936422-33-1
Molecular Formula:	C ₂₇ H ₃₃ F ₂ N ₇ O ₂
Molecular Weight:	525.59
Target:	Epigenetic Reader Domain; Histone Acetyltransferase
Pathway:	Epigenetics
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 2 years; -20°C, 1 year (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (190.26 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	1.9026 mL	9.5131 mL	19.0262 mL
	5 mM	0.3805 mL	1.9026 mL	3.8052 mL
	10 mM	0.1903 mL	0.9513 mL	1.9026 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
Solubility: ≥ 2.87 mg/mL (5.46 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
Solubility: 2.87 mg/mL (5.46 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 1.67 mg/mL (3.18 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 1.67 mg/mL (3.18 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 1.67 mg/mL (3.18 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GNE-781 is an orally active, highly potent and selective CBP inhibitor with an IC₅₀ of 0.94 nM in TR-FRET assay. GNE-781 also inhibits BRET and BRD4(1) with IC₅₀s of 6.2 nM and 5100 nM, respectively. GNE-781 displays antitumor activity in an MOLM-16 AML xenograft model^[1].

IC₅₀ & Target	IC50: 0.94 nM (CBP), 6.2 nM (BRET), 5100 nM (BRD4(1)) ^[1]
In Vitro	<p>GNE-781 is a highly advanced potent and selective bromodomain inhibitor of cyclic adenosine monophosphate response element binding protein, binding protein (CBP). GNE-781 reduces FOXP3 (forkhead box P3) transcript levels. Examination of a subset of bromodomains reveals that GNE-781 is exquisitely selective for CBP/P300 and is remarkably selective for CBP (5425-fold) and P300 (4250-fold). GNE-781 demonstrates an appropriate balance of cell potency, selectivity (5425-fold over BRD4(1))^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>GNE-781 (3-30 mg/kg; p.o.; twice daily for 21 days) has tumor growth inhibition (%TGI) is 73%, 71%, and 89% at 3, 10, and 30 mg/kg, respectively in SCID beige mice with MOLM-16 AML xenografts^[1].</p> <p>GNE-781 decreases Foxp3 transcript levels in a dose dependent manner. GNE-781 (3-30 mg/kg) suppresses MYC at doses as low as 3 mg/kg at 2 and 8 h, with maximal suppression at 10 and 30 mg/kg at 2 h (87% and 88% inhibition, respectively)^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

PROTOCOL

Animal Administration^[1]

Mice^[1]

Twelve female CD-1 mice are used. All animals are 6-9 weeks old at the time of study and weighed between 20 and 35 g. Animals (n=3 per dosing route) are dosed with 10 or GNE-781 at 1 mg/kg iv (in propyl ethylene glycol 400 (35% v/v) and water (65% v/v)) or 5 mg/kg po (suspended in 0.5% w/v methylcellulose, 0.2% w/v Tween 80). Food and water are available ad libitum to all animals. Serial blood samples (15 µL) are collected by tail nick at 0.033, 0.083, 0.25, 0.5, 1, 3, 8, and 24 h after the intravenous administration and 0.083, 0.25, 0.5, 1, 3, 8, and 24 h after the oral administration. All blood samples are diluted with 60 µL of water containing 1.7 mg/mL EDTA and kept at -80 °C until analysis^[1].

Rats^[1]

Twelve male Sprague-Dawley rats are used. All animals are 6-9 weeks old at the time of study and weighed between 200 and 300 g. Animals (n=3 per dosing route) are dosed with 10 or GNE-781 at 1 mg/kg iv (in propyl ethylene glycol 400 (35% v/v) and water (65% v/v)) or 5 mg/kg po (suspended in 0.5% w/v methylcellulose, 0.2% w/v Tween 80). Food and water are available ad libitum to animals in the iv groups. Animals in po groups are fasted overnight and food withheld until 4 h postdose. Approximately 250 µL of blood are collected via the catheter at 0.033, 0.083, 0.25, 0.5, 1, 2, 4, 8, and 24 h after the intravenous or oral administration. All blood samples are collected into tubes containing 5 µL of 0.5 M K₂EDTA and processed for plasma. Samples are centrifuged (2500g for 15 min at 4°C) within 1 h of collection, and plasma samples are kept at -80 °C until analysis^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Chem Biol. 2020 Dec 31;S2451-9456(20)30513-4.
- Patent. US20230255966A1.

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REFERENCES

[1]. Romero FA, et al. GNE-781, A Highly Advanced Potent and Selective Bromodomain Inhibitor of Cyclic Adenosine Monophosphate Response Element Binding Protein, Binding Protein (CBP). J Med Chem. 2017 Nov 22;60(22):9162-9183.

Caution: Product has not been fully validated for medical applications. For research use only.

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